

Initial REMS approval: 12/2012

Last modified/revised: 03/2017

**NDA 203858 JUXTAPID® (lomitapide)
Microsomal Triglyceride Transfer Protein Inhibitor**

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RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL

The goal of the JUXTAPID REMS is to mitigate the risk of hepatotoxicity associated with the use of JUXTAPID by ensuring that:

- Prescribers are educated about the approved indication for JUXTAPID, the risk of hepatotoxicity associated with the use of JUXTAPID; and the need to monitor patients during treatment with JUXTAPID as per product labeling.
- JUXTAPID is dispensed only to patients with a clinical or laboratory diagnosis consistent with homozygous familial hypercholesterolemia (HoFH).
- Patients are informed about the risk of hepatotoxicity associated with the use of JUXTAPID and the need for baseline and periodic monitoring.

II. REMS ELEMENTS

A. Elements to Assure Safe Use

1. Healthcare Providers (HCP) who prescribe JUXTAPID must be certified.

- a. To become certified to prescribe JUXTAPID, healthcare providers must:
 - i. Review the Prescribing Information for JUXTAPID.
 - ii. Review the *JUXTAPID REMS Program Fact Sheet*.
 - iii. Complete the *JUXTAPID REMS Program Prescriber Training Module* and successfully complete the *Knowledge Assessment*.
 - iv. Enroll in the JUXTAPID REMS Program by completing the *JUXTAPID REMS Program Prescriber Enrollment Form* and submitting it to the JUXTAPID REMS Program.

- b. As a condition of certification, prescribers must:
- i. Review the *JUXTAPID REMS Program Patient Guide* with each patient to counsel the patient about the appropriate use and risks associated with JUXTAPID and provide the patient a copy.
 - ii. Complete the *JUXTAPID REMS Program Patient-Prescriber Acknowledgement Form* for each patient and submit to the JUXTAPID REMS Program Coordinating Center.
 - iii. Perform the following on an ongoing basis for each patient: Complete and submit a *JUXTAPID REMS Program Prescription Authorization Form* for each new JUXTAPID prescription.
- c. Aegerion must:
- i. Ensure that healthcare providers who prescribe JUXTAPID are certified, in accordance with the requirements described above.
 - ii. Provide all of the following mechanisms for healthcare providers to complete the certification process for the JUXTAPID REMS Program: email and fax.
 - iii. Ensure that healthcare providers are notified when they have been certified by the JUXTAPID REMS Program.
 - iv. Maintain a validated, secure database of healthcare providers who are certified to prescribe JUXTAPID in the JUXTAPID REMS Program.
 - v. Ensure that healthcare providers meet the REMS requirements and de-certify healthcare providers who do not maintain compliance with REMS requirements.
 - vi. Provide the *JUXTAPID REMS Program Fact Sheet*, *JUXTAPID REMS Program Prescriber Training Module*, *JUXTAPID REMS Program Patient Guide*, *JUXTAPID REMS Program Patient-Prescriber Acknowledgement Form*, *JUXTAPID REMS Program Prescription Authorization Form* and the JUXTAPID Prescribing Information to healthcare providers who (1) attempt to prescribe JUXTAPID and are not yet certified, or (2) inquire about how to become certified.
 - vii. Send a *REMS Letter for Healthcare Providers* within 60 calendar days of the approval of the REMS modification (01/03/2017) to certified prescribers. The letter must be accompanied by the *JUXTAPID REMS Program Fact Sheet* and the Prescribing Information. The *REMS Letter* must also be available from the JUXTAPID REMS Program Website (www.juxtapidREMSprogram.com) at the time of the mailing, remain on the website for 6 months after the mailing and can be requested from the JUXTAPID REMS Program by phone at 1-85-JUXTAPID (1-855-898-2743).

The following materials are part of the REMS and are appended:

- *JUXTAPID REMS Program Prescriber Enrollment Form*
- *JUXTAPID REMS Program Prescriber Training Module and Knowledge Assessment*
- *JUXTAPID REMS Program Fact Sheet*
- *JUXTAPID REMS Program Patient Guide*
- *JUXTAPID REMS Program Patient-Prescriber Acknowledgement Form*
- *JUXTAPID REMS Program Prescription Authorization Form*
- *JUXTAPID REMS Letter for Healthcare Providers*
- *JUXTAPID REMS Program Website (www.juxtapidREMSprogram.com)*

2. Pharmacies that dispense JUXTAPID must be certified.

- a. To become certified to dispense JUXTAPID, pharmacies must:
 - i. Designate an authorized representative to complete the certification process by submitting the completed *JUXTAPID REMS Program Pharmacy Enrollment Form* on behalf of the pharmacy.
 - ii. Ensure that the authorized representative oversees implementation and compliance with the JUXTAPID REMS Program requirements by the following:
 - 1) Review the Prescribing Information.
 - 2) Review the *JUXTAPID REMS Program Fact Sheet*.
 - 3) Complete the *JUXTAPID REMS Program Pharmacy Training Module* and successfully complete the *Knowledge Assessment*.
 - 4) Ensure all relevant staff involved in the dispensing of JUXTAPID are trained on the JUXTAPID REMS Program requirements as described in the *JUXTAPID REMS Program Pharmacy Training Module* and maintain a record of training.
 - 5) Put processes and procedures in place to ensure the following requirements are completed prior to dispensing JUXTAPID:
 - a) Verify the *JUXTAPID REMS Program Patient-Prescriber Acknowledgement Form* is completed by accessing the JUXTAPID REMS Program database or by calling the JUXTAPID REMS Program Coordinating Center for verification.
 - b) Verify the prescriber is certified in the JUXTAPID REMS Program by accessing the JUXTAPID REMS Program database or by calling the JUXTAPID REMS Program Coordinating Center for verification.
 - c) Verify a *JUXTAPID REMS Program Prescription Authorization Form* is received for each new JUXTAPID prescription.

b. As a condition of certification:

- i. The certified pharmacy must recertify in the JUXTAPID REMS Program if a pharmacy designates a new authorized representative.
- ii. Maintain documentation that all processes and procedures are in place and are being followed for the JUXTAPID REMS Program and provide upon request to Aegerion, FDA, or a third party acting on behalf of Aegerion or FDA.
- iii. Comply with audits by Aegerion, FDA, or a third party acting on behalf of Aegerion or FDA to ensure that all processes and procedures are in place and are being followed for the JUXTAPID REMS Program.
- iv. Provide prescription data to Aegerion.

c. Aegerion must:

- i. Ensure that pharmacies that dispense JUXTAPID are certified, in accordance with the requirements described above.
- ii. Provide all the following mechanisms for pharmacies to complete certification for the JUXTAPID REMS Program: email and fax.
- iii. Ensure that pharmacies are notified when they have been certified by the JUXTAPID REMS Program.
- iv. Ensure that certified pharmacies are provided access to a database of certified prescribers, and patients who have a completed *JUXTAPID REMS Program Patient-Prescriber Acknowledgement Form*.
- v. Verify every 12 months that the authorized representative's name and contact information corresponds to that of the current designated authorized representative for the certified pharmacy. If different, the pharmacy must be required to re-certify with a new authorized representative.
- vi. Send a *REMS Letter for Pharmacists* within 60 calendar days of the approval of the REMS modification (01/03/2017). The letter must be accompanied by the *JUXTAPID REMS Program Fact Sheet* and the Prescribing Information.

The following materials are part of the REMS and are appended:

- *JUXTAPID REMS Program Pharmacy Training Module* and *Knowledge Assessment*
- *JUXTAPID REMS Program Pharmacy Enrollment Form*
- *JUXTAPID REMS Letter for Pharmacists*

3. JXTAPID must only be dispensed to patients with evidence or other documentation of safe-use conditions.

- a. Patients/caregivers must sign a *JXTAPID REMS Program Patient-Prescriber Acknowledgement Form* indicating that he/she has:
 - i. Received and has read the *JXTAPID REMS Program Patient Guide*
 - ii. Received counselling from the prescriber regarding:
 - 1) the risk of hepatotoxicity
 - 2) periodic liver function monitoring
 - 3) appropriate patient selection
- b. To authorize a patient to receive JXTAPID under the JXTAPID REMS Program, a certified prescriber must complete a *JXTAPID REMS Program Prescription Authorization Form* for each new JXTAPID prescription.
- c. Aegerion must:
 - i. Provide all of the following mechanisms for the certified prescriber to be able to submit the completed *JXTAPID REMS Program Patient-Prescriber Acknowledgement Form* to the JXTAPID REMS Program: email and fax.
 - ii. Ensure that the certified pharmacies complete the verifications required under [Section A.2](#) for patients prior to dispensing.
 - iii. Ensure that the certified pharmacies are able to verify JXTAPID is dispensed to patients only if there is evidence or other documentation that they have met the following requirements:
 - 1) Patient's *JXTAPID REMS Program Patient-Prescriber Acknowledgement Form* is completed
 - 2) Prescriber is certified
 - 3) *JXTAPID REMS Program Prescription Authorization Form* is received for each new JXTAPID prescription

B. Implementation System

- 1. Aegerion must ensure that JXTAPID is only distributed to certified pharmacies by:
 - a. Ensuring that wholesalers/distributors who distribute JXTAPID comply with the program requirements for wholesalers/distributors. The wholesaler/distributor must:
 - i. Put processes and procedures in place to verify, prior to distributing JXTAPID that the pharmacies are certified.

- ii. Train all relevant staff on the JUXTAPID REMS Program requirements.
 - iii. Comply with audits by Aegerion, FDA, or a third party acting on behalf of Aegerion or FDA to ensure that all processes and procedures are in place and are being followed for the JUXTAPID REMS Program. In addition, wholesalers/distributors must maintain documentation to support that all processes and procedures are in place, are being followed, and make the documentation available for audits.
 - iv. Provide distribution data to Aegerion to verify compliance with the JUXTAPID REMS Program.
 - b. Ensuring that wholesaler/distributors maintain distribution records of all shipments of JUXTAPID and provide the data to the JUXTAPID REMS Program.
2. Aegerion must monitor distribution data to ensure all the processes and procedures are in place and functioning to support the requirements of the JUXTAPID REMS Program.
 3. Aegerion must audit the wholesalers/distributors within 60 calendar days after the wholesaler/distributor is authorized to ensure that all processes and procedures are in place and functioning to support the requirements of the JUXTAPID REMS Program. Corrective action must be instituted by Aegerion if noncompliance is identified.
 4. Aegerion must maintain a validated, secure database of certified pharmacies and prescribers in the JUXTAPID REMS Program.
 5. Aegerion must maintain a validated, secure database of patients who have a completed *JUXTAPID REMS Program Patient-Prescriber Acknowledgement Form*.
 6. Aegerion must maintain records of JUXTAPID distribution and dispensing, certified prescribers, certified pharmacies, wholesalers/distributors, and patients who have a completed *Juxtapid REMS Program Patient-Prescriber Acknowledgement Form* to meet REMS requirements.
 7. Aegerion must maintain a JUXTAPID REMS Program Call Center 1-85-JUXTAPID (1-855-898-2743) and the JUXTAPID REMS Program Website (www.juxtapidREMSprogram.com). The REMS Program Website must include the capability to complete the prescriber and pharmacy *Knowledge Assessments* online, the option to print the PI, Medication Guide, and JUXTAPID REMS materials. The JUXTAPID product website must include a prominent REMS-specific link to JUXTAPID REMS Program Website. The JUXTAPID REMS Program Website must not link back to the product website(s).
 8. Aegerion must ensure the JUXTAPID REMS Program Website is fully operational and the REMS materials listed in or appended to the JUXTAPID REMS document are available through the JUXTAPID REMS Program Website and by calling the JUXTAPID REMS Program Call Center.
 9. Aegerion must monitor on an ongoing basis the certified pharmacies to ensure the requirements of the JUXTAPID REMS Program are being met. Aegerion must institute corrective action if noncompliance is identified and decertify pharmacies that do not maintain compliance with the JUXTAPID REMS Program requirements.
 10. Aegerion must maintain an ongoing annual audit plan and conduct annual audits that involves wholesalers, distributors, and pharmacies.

11. Aegerion must audit all certified pharmacies within 60 calendar days after the pharmacy is certified to ensure that all processes and procedures are in place and functioning to support the requirements of the JUXTAPID REMS Program. The certified pharmacies must also be included in Aegerion's ongoing annual audit plan. Aegerion must institute corrective action if noncompliance is identified.
12. Aegerion must take reasonable steps to improve implementation of and compliance with the requirements in the JUXTAPID REMS Program based on monitoring and evaluation of the JUXTAPID REMS Program.

III. Timetable for Submission of Assessments

Aegerion must submit REMS assessments to the FDA at 6 months, 12 months, and annually from the date of the initial approval of the REMS (12/21/2012). To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment. Aegerion must submit each assessment so that it will be received by the FDA on or before the due date.

Appendix 1: REMS Materials

- **PRESCRIBER ENROLLMENT FORM**
- **PRESCRIBER TRAINING MODULE AND KNOWLEDGE ASSESSMENT**
- **FACT SHEET**
- **PATIENT GUIDE**
- **PATIENT-PRESCRIBER ACKNOWLEDGMENT FORM**
- **PRESCRIPTION AUTHORIZATION FORM**
- **LETTER FOR HEALTHCARE PROVIDERS**
- **WEBSITE**
- **PHARMACY TRAINING MODULE AND KNOWLEDGE ASSESSMENT**
- **PHARMACY ENROLLMENT FORM**
- **LETTER FOR PHARMACISTS**